L5 ANSWER 29 OF 48 MEDLINE
AN 1999047297 MEDLINE
DN 99047297 PubMed ID: 9831402
TI Thrombophilia and inflammatory bowel disease: does factor V mutation have a role?.
AU Over H H; Ulgen S; Tuglular T; Tezel A; Avsar E; Geyik G; Basgul S; Sayhan N; Ulusoy N; Kalayci C; Tozun N
CS Marmara University Medical School, Department of Gastroenterology, Istanbul, Turkey.
SO EUROPEAN JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, (1998 Oct) 10 (10) 827-9.
Journal code: 9000874. ISSN: 0954-691X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199901
ED Entered STN: 19990209
Last Updated on STN: 19990209
Entered Medline: 19990127
AB BACKGROUND: An increased tendency for thromboembolism is a well known problem of inflammatory bowel disease (IBD). Microvascular thrombosis has also been claimed as a pathogenic factor in IBD. Recently a point **mutation** in the gene coding factor V (FV Leiden) has been identified in various thromboembolic diseases, but the role in IBD is unknown. OBJECTIVE: To determine the frequency of FV Leiden in IBD patients and compare with a group of controls. METHODS: Sixty-three IBD patients [43 **ulcerative colitis** (**UC**) patients and 20 Crohn's disease (**CD**) patients] and 36 healthy controls were included in the study. Only one of the **UC** patients had a history of cerebral thromboembolism. The extracted DNA from frozen blood was subjected to polymerase chain reaction for the amplification of FV gene. The amplicons were hybridized both with the mutant and wild-type probes to detect FV **mutation**. Readings of optical density above 0.3 were considered as positive results. According to the patterns of ELISA, heterozygosity and homozygosity for normal and mutant alleles were determined. RESULTS: Eight (18%) of **UC** patients were heterozygous normal and one (2%) patient had homozygous **mutation**. Eight (45%) of the 20 **CD** patients had a heterozygous pattern and one (5%) had a homozygous pattern. In the control group four (11%) subjects showed a heterozygous genotype. FV Leiden was found to be statistically more frequent in **CD** patients ($P < 0.005$) (odds ratio 6.5, 95% confidence interval 1.3-18.), but not in the **UC** patients as compared with controls ($P > 0.05$). There was no significant correlation between FV Leiden presence and disease activity, gender or disease duration for both **UC** and **CD**. CONCLUSION: The results suggest that FV Leiden is more frequent in **CD** patients, but not in the **UC** patients as compared with controls. The high rate of factor V **mutation** in our **CD** patients suggests the need for further studies to confirm a relationship between this **mutation** and aetiology of the disease.

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L5 ANSWER 15 OF 48 MEDLINE
AN 2001043559 MEDLINE
DN 20546215 PubMed ID: 11093274
TI Combined segregation and linkage analysis of inflammatory bowel disease in the IBD1 region using severity to characterise Crohn's disease and ulcerative colitis. On behalf of the GISC.
AU Forabosco P; Collins A; Latiano A; Annese V; Clementi M; Andriulli A; Fortina P; Devoto M; Morton N E
CS Istituto di Genetica Molecolare CNR, Alghero, Italy.. paola@genet3.unimo.it
SO EUROPEAN JOURNAL OF HUMAN GENETICS, (2000 Nov) 8 (11) 846-52. Journal code: 9302235. ISSN: 1018-4813.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200012
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001207
AB Inflammatory bowel disease (IBD) is a chronic relapsing disorder affecting the gastro-intestinal tract and is subdivided into two main subtypes: Crohn's disease (**CD**) and **ulcerative colitis** (**UC**). Although the aetiology of IBD is unknown, a strong genetic susceptibility is suggested and different candidate regions have been identified for both **CD** and **UC**. The IBD1 region on chromosome 16 has been confirmed to be important for susceptibility to **CD**, whereas conflicting evidence has been obtained for **UC**. We performed a combined linkage and segregation analysis in the identified IBD1 region on a sample of 82 extended families with IBD using a parametric method implemented in the computer program COMDS. This approach allows simultaneous evaluation of linkage while estimating the mode of inheritance and to include severity of the trait to characterise the **CD** and **UC** phenotypes. Our results are consistent with the presence of a major gene in the IBD1 region close to D16S408 involved in both **UC** and **CD**. Furthermore, our data support evidence that a single **mutation** in the gene leads more frequently to **UC**, whereas inheritance of two mutant alleles results in the more severe **CD**. In our study the IBD1 locus was found to have a major role in IBD predisposition in the Italian population.

L5 ANSWER 31 OF 48 MEDLINE
AN 1998217106 MEDLINE
DN 98217106 PubMed ID: 9558024
TI Polymorphism of motilin gene in patients with Crohn's disease.
AU Annese V; Piepoli A; Andriulli A; Napolitano G; Bisceglia L; Zelante L; Gasparini P
CS Division of Gastroenterology, C.S.S. Hospital, I.R.C.C.S., San Giovanni Rotondo, Italy.
SO DIGESTIVE DISEASES AND SCIENCES, (1998 Apr) 43 (4) 715-9.
Journal code: 7902782. ISSN: 0163-2116.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199805
ED Entered STN: 19980514
Last Updated on STN: 19980514
Entered Medline: 19980505
AB An increasing body of evidence supports the concept of genetic heterogeneity within inflammatory bowel disease (IBD). In this study, a **polymorphism** of the motilin gene, which determines an amino acid substitution in the motilin protein, has been investigated in IBD patients. Fifty patients with **ulcerative colitis** (**UC**), and 52 with Crohn's disease (**CD**) were investigated for anti-neutrophil cytoplasmatic antibodies (ANCA) and the **polymorphism** in the second exon of the motilin gene. Sixty unrelated blood donors served as controls. ANCA were found in 30% of **UC** and 13% of **CD**. In controls the DNA **polymorphism** identified two alleles (1 and 2) at a frequency of 42% and 58%, respectively. Patients with either **UC** or **CD** showed a slight increase in the frequency of allele 2 (69% and 60%, respectively; $P > 0.05$ vs controls). This allele was predominant in ANCA-positive **CD** patients (86%; $P < 0.04$) while in **UC** it did not differ. All ANCA-positive **CD** patients had the disease confined to the colon. A **polymorphism** of second exon of the motilin gene, leading to a protein variant, is significantly more frequent in the subset of ANCA-positive **CD** patients. This subgroup of patients appears to share peculiar genetic and clinical features.

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L6 ANSWER 4 OF 48 MEDLINE
AN 2002151994 MEDLINE
DN 21881236 PubMed ID: 11875755
TI CARD15/NOD2 mutational analysis and genotype-phenotype correlation in 612 patients with inflammatory bowel disease.
AU Lesage Suzanne; Zouali Habib; Cezard Jean-Pierre; Colombel Jean-Frederic; Belaiche Jacques; Almer Sven; Tysk Curt; O'Morain Colm; Gassull Miquel; Binder Vibeke; Finkel Yigael; Modigliani Robert; Gower-Rousseau Corinne; Macry Jeanne; Merlin Francoise; Chamaillard Mathias; Jannot Anne-Sophie; Thomas Gilles; Hugot Jean-Pierre
CS Fondation Jean Dausset-CEPH, 27 rue Juliette Dodu, 75010 Paris, France. (EPWG-IBD Group; EPIMAD Group; GETAID Group).
SO AMERICAN JOURNAL OF HUMAN GENETICS, (2002 Apr) 70 (4) 845-57. Journal code: 0370475. ISSN: 0002-9297.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF178930; GENBANK-AJ303140; OMIM-MIM191390; OMIM-MIM266600
EM 200204
ED Entered STN: 20020311
Last Updated on STN: 20020419
Entered Medline: 20020418
AB CARD15/NOD2 encodes a protein involved in bacterial recognition by monocytes. **Mutations** in CARD15 have recently been found in patients with Crohn disease (**CD**), a chronic inflammatory condition of the digestive tract. Here, we report the mutational analyses of CARD15 in 453 patients with **CD**, including 166 sporadic and 287 familial cases, 159 patients with **ulcerative colitis** (**UC**), and 103 healthy control subjects. Of 67 sequence variations identified, 9 had an allele frequency >5% in patients with **CD**. Six of them were considered to be **polymorphisms**, and three (R702W, G908R, and 1007fs) were confirmed to be independently associated with susceptibility to **CD**. Also considered as potential disease-causing **mutations** (DCMs) were 27 rare additional **mutations**. The three main variants (R702W, G908R, and 1007fs) represented 32%, 18%, and 31%, respectively, of the total **CD mutations**, whereas the total of the 27 rare **mutations** represented 19% of DCMs. Altogether, 93% of the **mutations** were located in the distal third of the gene. No **mutations** were found to be associated with **UC**. In contrast, 50% of patients with **CD** carried at least one DCM, including 17% who had a double **mutation**. This observation confirmed the gene-dosage effect in **CD**. The patients with double-dose **mutations** were characterized by a younger age at onset (16.9 years vs. 19.8 years; P=.01), a more frequent stricturing phenotype (53% vs. 28%; P=.00003; odds ratio 2.92), and a less frequent colonic involvement (43% vs. 62%; P=.003; odds ratio 0.44) than were seen in those patients who had no **mutation**. The severity of the disease and extraintestinal manifestations were not different for any of the CARD15 genotypes. The proportion of familial and sporadic cases and the proportion of patients with smoking habits were similar in the groups of patients with **CD** with or without **mutation**. These findings provide tools for a DNA-based test of susceptibility and for genetic counseling in inflammatory bowel disease.

AN 2002195622 MEDLINE
DN 21906773 PubMed ID: 11910337
TI The contribution of NOD2 gene mutations to the risk and site of disease in inflammatory bowel disease.
CM Comment in: Gastroenterology. 2002 Apr;122(4):1161-2
AU Cuthbert Andrew P; Fisher Sheila A; Mirza Muddassar M; King Kathy; Hampe Jochen; Croucher Peter J P; Mascheretti Silvia; Sanderson Jeremy; Forbes Alastair; Mansfield John; Schreiber Stefan; Lewis Cathryn M; Mathew Christopher G
CS Division of Medical and Molecular Genetics, Guy's, King's, and St Thomas' School of Medicine, London, England, United Kingdom.
SO GASTROENTEROLOGY, (2002 Apr) 122 (4) 867-74.
Journal code: 0374630. ISSN: 0016-5085.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200204
ED Entered STN: 20020404
Last Updated on STN: 20020419
Entered Medline: 20020418
AB BACKGROUND & AIMS: **Mutations** in the NOD2 gene are strongly associated with susceptibility to Crohn's disease (**CD**). We analyzed a large cohort of European patients with inflammatory bowel disease to determine which **mutations** confer susceptibility, the degree of risk conferred, their prevalence in familial and sporadic forms of the disease, and whether they are associated with site of disease. METHODS: Individuals were genotyped for 4 NOD2 **mutations**: P268S, R702W, G908R, and 3020insC. Allelic transmission distortion to 531 **CD**- and 337 **ulcerative colitis**-affected offspring was assessed by the transmission disequilibrium test. Association was also tested in an independent cohort of 995 patients with inflammatory bowel disease and 290 controls. Cases were stratified by disease site and compared across NOD2 genotypes. RESULTS: R702W, G908R, and 3020insC were strongly associated with **CD** but not with **ulcerative colitis**. Linkage disequilibrium was observed between P268S and the other **mutations**, forming 3 independent disease haplotypes. Genotype relative risks were 3.0 for **mutation** heterozygotes and 23.4 for homozygotes or compound heterozygotes. The frequency of NOD2 **mutations** was higher in cases from families affected only with **CD** and was significantly increased in ileal-specific disease cases compared with colon-specific disease (26.9% vs. 12.7%, P = 0.0004). CONCLUSIONS: The R702W, G908R, and 3020insC **mutations** are strong independent risk factors for **CD** and are associated particularly with ileal disease.

(FILE 'HOME' ENTERED AT 11:55:47 ON 20 AUG 2002)

FILE 'MEDLINE, CAPLUS' ENTERED AT 11:55:54 ON 20 AUG 2002

L1 0 S ASSOCIATED (10A) "CROHN'S DISEASE" (10A) "NOT" (10A) ULCERATI
L2 0 S ASSOCIATED (P) "CROHN'S DISEASE" (P) "NOT" (P) ULCERATIVE COL
L3 0 S ASSOCIATED (P) CD (P) "NOT" (P) UC
L4 1094 S (ULCERATIVE COLITIS OR UC) (P) ("CROHN'S DISEASE" OR CD)
L5 899 DUP REM L4 (195 DUPLICATES REMOVED)
L6 48 S L5 (P) (POLYMORPHISM OR POLYMORPHISMS OR MUTATION OR MUTATIO